Claims (clean version of new claims)

What is claimed is:

35. (new) A method of magnetic resonance investigation of a sample, preferably of a human or non-human animal body, said method comprising:

(i) nuclear spin polarising a solid MR imaging agent;

(ii) administering the nuclear spin polarised MR imaging agent to said sample;

(iii) exposing said sample to a radiation at a frequency selected to excite nuclear spin transitions in the spin polarised nuclei of the MR imaging agent;

(iv) detecting magnetic resonance signals from said sample; and

(v) generating an image, dynamic flow data, diffusion data, perfusion data, physiological data or metabolic data from said detected signals,

wherein said polarising step (i) is carried out by

(a) spin refrigeration, or by,

(b) irradiating with circularly polarised light.

36. (new) The method of claim 35 wherein said agent is administered to said sample after dissolution in water.

37. (new) The method of claim 35 wherein said agent further comprises other pharmaceutical additives.

09960512.111601

38. (new) The method of claim 35 wherein said solid MR imaging agent is a water-soluble high T_1 agent.

39. (new) The method of claim 35 wherein said MR imaging agent retains its polarisation when transported in a substantially uniform magnetic field and at a low temperature.

40. (new) The method of claim 39 wherein said magnetic field is greater than 10 mT.

41. (new) The method of claim 39 wherein said magnetic field is greater than 1T.

42. (new) The method of claim 39 wherein said temperature is lower than 80°K.

43. (new) The method of claim 39 wherein said temperature is lower than 4.2°K.

44. (new) The method of claim 36 wherein a magnetic field is present during the dissolution stage.

45. (new) The method of claim 35 wherein step (i) comprises:

(i) irradiating a solid compound having a singlet electronic ground state and containing a non zero nuclear spin nucleus with light to generate an excited polarized triplet electronic state of said agent;

0990512.111601

(ii) transforming electronic polarization of said solid compound into a nuclear spin polarization in a soluble MR imaging agent to form a nuclear spin polarised MR imaging agent;

(iii) dissolving said polarised MR imaging agent in an aqueous medium.

46. (new) The method of claim 35 wherein said step (ii) is carried out after the MR imaging agent is dissolved in a physiologically tolerable solvent.

47. (new) The method of claim 35 wherein said step (ii) is carried out after the MR imaging agent is separated from some or all of the paramagnetic species or chromophores.

09990512.111601

48. (new) The method of claim 46 wherein the solution formed retains its polarisation in frozen form.

49. (new) An apparatus for use in the method of claim 35 when the polarising of a MR agent is by spin refrigeration, the apparatus comprising:

(i) a chamber cooled to a temperature preferably lower than 80K disposed in the primary magnetic field of MR apparatus, or in a separate magnetic field, of strength 0.2T or more;

and wherein said chamber is:

(i) adapted to receive particulate solid MR imaging agent, doped with or intimately mixed with paramagnetic polarising agent;

(ii) rotates said agent about an axis non-parallel with the primary field or passes said agent through a conduit such that it rotates in that way or mixes said agent such that it rotates in that way, or, where the chamber is in a separate magnetic field, rotates the magnetic field about one or more axes;

(iii) dissolves said polarised solid agent in or passes it to a mixing chamber, where it is dissolved in a physiologically tolerable solvent;

(iv) passes the solution thus formed through or over an immobilised paramagnetic metal binding agent and/or through a filter;

(v) and into the conduit for administration into a sample situated within the primary magnetic field of the MR imager.

50. (new) The apparatus of claim 49 wherein said chamber is cooled to lower than or equal to 1°K.

51. (new) The apparatus of claim 49 wherein the strength of said magnetic field is 0.5 to 10T.

52. (new) A process for the preparation of a nuclear spin polarised MR imaging agent, said process comprising:

irradiating a solid compound having a singlet electronic ground state and containing a non zero nuclear spin nucleus with light to generate an excited polarized triplet electronic state of said agent;

transforming electronic polarization of said solid compound into a nuclear spin polarization in a soluble solid MR imaging agent to form a nuclear spin polarised MR imaging agent, optionally dissolving said MR imaging agent in an aqueous medium (preferably a physiologically tolerable medium), and optionally storing said polarised MR imaging agent at a reduced temperature and at a magnetic field of greater than 10 mT.

53. (new) The process of claim 52 wherein said reduced temperature is liquid nitrogen temperature or below.

54. (new) The process of claim 52 wherein said reduced temperature is liquid helium temperature.

55. (new) The process of claim 52 wherein said magnetic field is greater than 2T.

56. (new) A process for the preparation of a polarised electronic triplet state of a solid compound having a singlet electronic ground state said process comprising irradiating said compound in a solid state with a first radiation of a wavelength selected to excite said compound from a ground singlet electronic state to an excited singlet electronic state and with a positively or negatively, circularly polarised second radiation of a wavelength selected to excite said compound from the lowest triplet electronic state to the next-to-lowest triplet electronic state.

57. (new) The process of claim 56 wherein said compound is a water-soluble compound containing at least one non-zero nuclear spin nucleus.

58. (new) A water-soluble MR imaging agent compound:

(i) containing a nuclear spin polarised I=½ nucleus;

(ii) having a molecular weight below 1000D;

(iii) containing a cyclic chromophore; and

(iv) having an nmr spectrum for said I=½ nucleus having a linewidth of less than 100 Hz.

09596512.111601

59. (new) The agent compound of claim 58 wherein said molecular weight is below 500D.

60. (new) The agent of claim 58 wherein said cyclic chromophore is heterocyclic.

61. (new) The agent of claim 58 wherein said linewidth is below 1 Hz.

62. (new) A physiologically tolerable MR imaging composition comprising the nuclear spin polarised MR imaging agent of claim 58 dissolved in water together with one or more physiologically tolerable excipients, said imaging agent containing nuclei of a I=½ isotope characterised in that said nuclei are polarised such that their nmr signal intensity is equivalent to a signal intensity achievable in a magnetic field of at least 0.1T.

63. (new) The composition of claim 62 wherein said nuclei are at higher than natural abundance.

64. (new) The composition of claim 62 wherein said magnetic field is at least 450T.

65. (new) The composition of claim 62 wherein said composition is sterile and is stable at a physiological temperature.

66. (new) A method of manufacture of an MR imaging composition for use in a method of diagnosis involving generation of a MR image by MR imaging of a human or non-human animal body, wherein said method involves nuclear spin polarisation of an MR imaging agent by means of spin refrigeration.

09990512.111601